What is claimed is:

1. A substantially pure population of viable pancreatic progenitor cells characterized by expression of PDX1 and able to differentiate into glucose-responsive, insulin-secreting cells.

2. A cellular composition comprising, as the cellular component, a substantially pure population of viable pancreatic progenitor cells, which progenitor cells are capable of proliferation and/or differentiation in a culture medium.

3. The composition of claim 2, having fewer than 20% of lineage committed cells.

4. The composition of claim 2, which progenitor cells are from a mammal.

5. The composition of claim 4, which mammal is a transgenic mammal.

6. The composition of claim 4, which mammal is a primate.

7. The composition of claim 6, which mammal is a human.

8. The composition of claim 4, which mammal is a miniature swine.

9. The composition of claim 2, which progenitor cells are capable of differentiation to pancreatic lineages.

10. The composition of claim 9, which progenitor cells are capable of differentiation to β islet cells, ∝ cells, δ islet cells, ϕ islet cells, or exocrine cells.

11. The composition of claim 10, wherein the progenitor cells are characterized by expression of one or more of a hepatocyte nuclear factor (HNF); STF-1, PAX genes, PTF-1, hXBP-1, villin, tyrosine hydroxylase, insulin, glucagon, or neuropeptide Y.

12. The composition of claim 11, wherein the progenitor cells are characterized by expression of PAX-6.

13. The composition of claim 2, which progenitor cells can be maintained in culture for at least about 7 days.

14. A cellular composition comprising, as a cellular population, at least 75% progenitor cells being isolated from pancreatic ductal epithelium or are the progeny thereof, which progenitor cells are capable of self-regeneration in a culture medium.

15. A cellular composition consisting essentially of, as the cellular population, viable pancreatic progenitor cells capable of self-regeneration in a culture medium and differentiation to members of the pancreatic lineages.

16. The composition of claim 14, which progenitor cells are isolated from intralobular cells.

17. The composition of claim 15, which progenitor cells are responsive to one or more growth factor selected from a group consisting of IGF, EGF, TGF, FGF, HGF and VEGF, or orthologous or paralogous factors thereof.

18. A cellular composition comprising pancreatic progenitor cells, with fewer than 20% of lineage committed cells, which progenitor cells are capable of self-regeneration in a culture medium and differentiation to pancreatic lineages.

19. The composition of claim 18, which progenitor cells are inducible to differentiate into pancreatic islet cells.

20. The composition of claim 19, which islet cells are pancreatic β islet cells.

21. The composition of claim 19, which islet cells are pancreatic α islet cells.

22. The composition of claim 19, which islet cells are pancreatic δ islet cells.

23. The composition of claim 19, which islet cells are pancreatic ϕ islet cells.

24. The composition of claim 18, wherein the progenitor cells are characterized by expression of STF-1 and PAX6.

25. The composition of claim 18, further comprising an inducing agent.

26. The composition of claim 25, wherein said inducing agent is selected from the group consisting of Forskolin, Di-butyrl cAMP, Na-Butyrate, dexamethasone and cholera toxin

27. A pharmaceutical composition comprising the cellular composition of claim 2.

28. A pharmaceutical composition comprising the cellular composition of claim 15.

29. A pharmaceutical composition comprising the cellular composition of claim 16.

30. A pharmaceutical composition comprising the cellular composition of claim 18.

31. A method of isolating progenitor cells comprising:
    i) obtaining pancreatic ductal cells;
    ii) culturing said pancreatic cells in a suitable nutrient medium;
    iii) isolating a population of progenitor cells from said culture.

32. A method of claim 31, comprising obtaining pancreatic intralobular ductal epithelial cells.

33. A method of claim 31, wherein said pancreatic ductal epithelial cells are obtained by explant or by enzymatic digestion.

34. A method of claim 31, wherein said pancreatic ductal cells are grown to confluence.

35. A method of claim 31, wherein said progenitor cells are isolated by mechanical separation.

36. A method of claim 34, wherein after growing said culture to confluence non-adherent cells are isolated and further treated with an agent.

37. A method of claim 36, wherein said agent induces differentiation and is selected from the group consisting of Forskolin, Di-butyrl cAMP, Na-Butyrate, dexamethasone and cholera toxin.

38. A method of claim 36, wherein said agent is a growth factor.

39. A method of claim 38, wherein said growth factor is selected from a group consisting of IGF, TGF, FGF, EGF, HGF, hedgehog and VEGF.

40. A method of claim 38, wherein said growth factor is selected from a group consisting of the TGFβ superfamily, BMP2 and BMP7.

41. A cellular composition consisting essentially of, as the cellular population, viable pancreatic progenitor cells capable of self-regeneration in a culture medium and differentiation to members of the pancreatic lineages, which cells are isolated by the method comprising

obtaining dissociated epithelial cells from pancreatic ductss;

culturing, as a monolayer, the epithelial cells in a suitable nutrient medium to expand pancreatic progenitors from said epithelial cell monolayer;

isolating said progenitor cells from said culture.

42. A method for stimulating the *ex vivo* proliferation of mammalian pancreatic β-islet cells, comprising the steps of:

(a) preparing a primary culture of mammalian pancreatic cells; and,

(b) contacting said primary culture cells with an effective concentration of a cAMP agonist, wherein the effective concentration is an amount sufficient to induce the primary culture to differenitate to β-islet cells.

43. The method of claim 42, wherein the primary culture cells are human pancreatic cells.

44. The method of claim 41, wherein said cell differentiation comprises an increase in average cellular insulin production.

45. The method of claim 41, further comprising growing said cultured cells in monolayer on an extracellular matrix in the presence of a growth factor.

46. The method of claim 41, further comprising contacting said cells with an agent that upregulates the insulin gene, e.g., a poly (ADP-ribose) synthetase inhibitor such as nicotinamide or a benzamide.

47. A method for stimulating the ex vivo proliferation of human adult pancreatic beta - cells, comprising the steps of:

(a) preparing a monolayer culture of primary human adult pancreatic cells; and

(b) culturing said cells with an effective concentration of a growth factor and a cAMP agonist, wherein the effective concentration is an amount sufficient to induce the primary culture to produce insulin-producing cells.

48. A method for treating a subject suffering from, or at risk of developing, Type 1 diabetes mellitus, comprising the steps of:

(a) preparing a primary culture of human adult pancreatic cells;

(b) contacting said primary culture with a reagent comprising an effective concentration of a cAMP agonist, wherein the effective concentration is an amount sufficient to induce the primary culture to produce insulin-producing cells;

(c) harvesting the thus-treated adult pancreatic cells; and,

(d) transplanting in said subject an effective amount of said cells of part (c) above.

49. A method for treating a subject suffering from, or at risk of developing, Type 1 diabetes mellitus, comprising the steps of:

(a) contacting a primary culture of pancreatic cells with a reagent comprising an effective concentration of a cAMP agonist, wherein the effective concentration is an amount sufficient to induce the primary culture to produce insulin-producing;

(b) harvesting the thus-treated adult pancreatic cells; and,

(c) transplanting in said subject an effective amount of said cells of part (c) above.

50. The method of claim 48, wherein said parenterally transplanting comprises administering by an intraportal, intrasplenic, renal subcapsular route, or intravenous route.

51. The method of claim 48, wherein step b) further comprises growing said cells in monolayer culture in the presence of an effective concentration of a growth factor, e.g., the growth factor is selected from a group consisting of IGF, TGF, FGF, EGF, HGF, hedgehog, VEGF and a member of the TGFβ superfamily.

52. The method of claim 50, further comprising dissociating by non-enzymatic means said monolayer cells, then reaggregating said dissociated cells.

53. The method of claim 51, further comprising contacting said reaggregated cells with an agent that upregulates the insulin gene in said cells, e.g., a poly (ADP-ribose) synthetase inhibitor such as a nicotinamide or a benzamide.

54. A method of producing proliferating and differentiating human adult pancreatic islet cells in clinically useful quantities, comprising the steps of:

(a) seeding a bioreactor with a human pancreatic cell culture;

(b) perfusing said bioreactor with a complete growth medium supplemented with an amount of cAMP agonist sufficient to induce cells in the bioreactor to proliferate and differentiate into insulin-secreting cells; and

(c) harvesting insulin-secreting cells from said bioreactor.

SUB A2

55. A method for preparing a substantially pure non-adherent population of progenitor cells comprising:

obtaining a cell suspension from an animal tissue, wherein said cell suspension comprises at least one progenitor cell;

treating the cell suspension with a growth factor preparation; and

allowing proliferation of said at least one progenitor cell such that a substantially pure non-adherent progenitor cell population is obtained,

thereby obtaining a substantially pure non-adherent progenitor cell population.

56. The method of claim 55, wherein said non-adherent population of progenitor cells is at least about 50% pure.

SUB B7

57. The method of claim 55, wherein said non-adherent population of progenitor cells is at least about 60% pure.

58. The method of claim 55, wherein said non-adherent population of progenitor cells is at least about 70% pure.

59. The method of claim 55, wherein said non-adherent population of progenitor cells is at least about 80% pure.

60. The method of claim 55, wherein said non-adherent population of progenitor cells is at least about 90% pure.

61. The method of claim 55, wherein said animal tissue is obtained from a mammalian organ.

62. The method of claim 55, wherein said animal tissue is selected from the group consisting of: pancreatic tissue, liver tissue, smooth muscle tissue, striated muscle tissue, cardiac muscle tissue, bone tissue, bone marrow tissue, bone spongy tissue, cartilage tissue, liver tissue, pancreas tissue, pancreatic ductal tissue, spleen tissue, thymus tissue, tonsil tissue, Peyer's patch tissue, lymph nodes tissue, thyroid tissue, epidermis tissue, dermis tissue, subcutaneous tissue, heart tissue, lung tissue, vascular tissue,

endothelial tissue, blood cells, bladder tissue, kidney tissue, digestive tract tissue, esophagus tissue, stomach tissue, small intestine tissue, large intestine tissue, adipose tissue, uterus tissue, eye tissue, lung tissue, testicular tissue, ovarian tissue, prostate tissue, connective tissue, endocrine tissue, mesentery tissue, fetal tissue and umbilical tissue.

63. The method of claim 55, wherein said cell suspension is obtained by mechanical disruption of said animal tissue.

64. The method of claim 55, wherein said cell suspension is obtained by enzymatic disruption of said animal tissue.

SUB A3

65. The method of claim 55, wherein said growth factor preparation comprises at least one of: epidermal growth factor, transforming growth factor, hepatocyte growth factor, fibroblast growth factor, leukemia inhibitory factor, insulin-like growth factor and platelet-derived growth factor.

(sub B8)

66. The method of claim 55, wherein said substantially pure non-adherent progenitor cells are floating cells.

67. The method of claim 55, wherein said substantially pure non-adherent progenitor cells are non-adherent cells.

68. The method of claim 55, wherein said substantially pure non-adherent progenitor cells forms a homotypic cell sphere.

69. A method for preparing a substantially pure non-adherent population of progenitor cells comprising:

providing an animal tissue;

disrupting said animal tissue so as to obtain a cell suspension comprising at least one progenitor cell; and

allowing proliferation of said at least one progenitor cell such that a substantially pure non-adherent progenitor cell population is obtained,

thereby obtaining a substantially pure non-adherent progenitor cell population.

SUB A4

70. The method of claim 69, wherein said animal tissue is selected from the group consisting of: pancreatic tissue, liver tissue, smooth muscle tissue, striated muscle tissue, cardiac muscle tissue, bone tissue, bone marrow tissue, bone spongy tissue, cartilage tissue, liver tissue, pancreas tissue, pancreatic ductal tissue, spleen tissue, thymus tissue, tonsil tissue, Peyer's patch tissue, lymph nodes tissue, thyroid tissue, epidermis tissue, dermis tissue, subcutaneous tissue, heart tissue, lung tissue, vascular tissue, endothelial tissue, blood cells, bladder tissue, kidney tissue, digestive tract tissue, esophagus tissue, stomach tissue, small intestine tissue, large intestine tissue, adipose tissue, uterus tissue, eye tissue, lung tissue, testicular tissue, ovarian tissue, prostate tissue, connective tissue, endocrine tissue, mesentery tissue, fetal tissue and umbilical tissue

71. The method of claim 55 or 69, wherein said non-adherent progenitor cell population expresses Nestin.

72. The method of claim 55 or 69, wherein said non-adherent progenitor cell population expresses at least one: c-kit and Sca.

73. The method of claim 55 or 69, wherein said non-adherent progenitor cell population under proper conditions can give rise to cells that express a marker selected from the group comprising: Pdx-1, glucagon, and insulin.

74. A composition comprising the substantially-pure nonadherent progenitor cell population obtained by the method of claim 55 or 69.

75. The composition of claim 74, wherein the substantially-pure nonadherent progenitor cell population expresses a marker selected from the group consisting of: Nestin, c-kit and Sca.

76. The composition of claim 74, wherein the substantially-pure nonadherent progenitor cell population under proper conditions can give rise to cells that express a marker selected from the group comprising: Pdx-1, glucagon, and insulin.

77. The method of claim 55 or 69, wherein said substantially pure non-adherent population of progenitor cells is at least about one thousand-fold enriched from said animal cell suspension.

78. The method of claim 55 or 69, wherein said substantially pure non-adherent population of progenitor cells is at least about one hundred-fold enriched from said animal cell suspension.